REVIEW

Systematic Review and Meta-Analysis on the Effect of Portion Size and Ingestive Frequency on Energy Intake and Body Weight among Adults in Randomized Controlled Feeding Trials

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ABSTRACT

Energy intake is the product of portion size (PS)—the energy content of an ingestive event—and ingestive frequency (IF)—the number of ingestive events per unit time. An uncompensated alteration in either PS or IF would result in a change in energy intake and body weight if maintained over time. The objective of this meta-analysis was to assess the independent effects of PS and IF on energy intake and body weight among healthy adults in randomized controlled trials (RCTs). A total of 9708 articles were identified in PubMed, Web of Science, Cochrane, and CINAHL databases. The articles were divided among 10 researchers; each article was screened for eligibility by 2–3 independent reviewers. Exclusion criteria included: populations <19 y and >65 y, unhealthy populations (i.e. participants with an acute or chronic disease), assessments <24 h and <4 wk in duration for trials investigating energy intake or body weight, respectively. Controlled feeding trials (i.e. fixed energy intake) that manipulated IF and PS in the same study intervention (IF/PS) were evaluated separately and for the body weight outcome only. Twenty-two studies (IF = 4, PS = 14, IF/PS = 4) met the inclusion criteria. There was an insufficient number of studies to assess the effect of IF, PS, or IF/PS on body weight. There was heterogeneity in the effect sizes among all comparisons ($I^2 \geq 75\%$). Consuming larger portion sizes was associated with higher daily energy intake [295 kcal (202, 388), $n = 24$; weighted mean differences (WMD) (95% CI), $n =$ comparisons], and increased frequency of ingestive events was associated with higher energy intake [203 kcal (76, 330), $n = 10$]. Results from RCTs support that larger PS and greater IF are both associated with higher energy consumption. However, there is insufficient information to determine chronic effects on body weight. This protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO) as CRD42018104757. *Adv Nutr* 2022;13:248–268.

Statement of Significance: Results from this systematic review and meta-analysis reveal that both larger portion sizes and increased ingestive frequency are associated with higher total daily energy intake in randomized controlled trials among healthy adults, yet there were an insufficient number of published studies to determine whether the short-term increases in energy intake would influence body weight if maintained long term.

Keywords: ingestive behavior, serving size, food intake, feeding pattern, healthy population, normal weight, overweight, obese

Introduction

The high prevalence of obesity and severe obesity among the US population continues to be a major public health concern (1). Weight gain occurs as the result of a positive energy balance where energy intake exceeds energy expenditure. Total daily energy intake is the product of portion size (PS)—the energy content of an ingestive event—and ingestive frequency (IF)—the number of ingestive events per unit time. In recent decades, both PS (2, 3) and IF (4, 5) among adults have increased concurrently with the rise in obesity (6), suggesting that increasing PS and/or IF may result in chronic positive energy balance leading to body weight gain.

To maintain body weight via regulation of energy balance, an increase in PS would theoretically require a reduction in

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either PS at subsequent ingestive events and/or a reduction of 1 or more ingestive events. Conversely, an increase in IF within a specified time interval would necessitate a reduction in the PS of subsequent ingestive events to maintain energy balance. Strategies for moderating energy intake via manipulating PS and/or IF have been proposed (e.g. portion-controlled meals, intermittent fasting). However, changing dietary patterns to habitually consume an energy balanced diet or net negative energy diet have proven difficult to achieve among the general public. The relative efficacy of strategies to manipulate PS or IF for weight loss or weight maintenance remains unclear.

Therefore, the aim of this systematic review and meta-analysis was to determine if either PS or IF are predictors of energy intake and body weight. The primary objective was to independently assess the effects of either PS or IF on dietary energy intake and body weight among healthy individuals in randomized controlled trials (RCTs). We hypothesized that independent increases in PS or IF would increase energy intake in the short term, and thus could plausibly increase body weight in the long term.

Methods

This systematic review and meta-analysis followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) report outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (7). The procedures for identification, screening, data extraction, and analysis were agreed upon in advance among all authors. The research question was defined by using the PICOS (population, intervention, comparison, outcome, and setting) criteria (**Table 1**). Details of methods were documented in a protocol that was registered at the International Prospective Register of Systematic Reviews (PROSPERO) as CRD42018104757 before literature search and analysis.

Inclusion Criteria

Randomized, parallel or crossover, controlled trials with apparently healthy participants (i.e. participants not characterized with an acute or chronic disease) with a BMI 18–40 kg/m^2, aged 19–65 y were included. Additionally, interventions were ≥24 h in duration for assessments of energy intake and ≥4 wk in duration for assessments of body weight. All trials must have included ≥1 treatment arm altering either IF or PS and a control (comparison) group. An ingestive event was considered any eating or drinking occasion that involved the intake of energy; examples include, but are not limited to, meals, snacks, caloric beverages. Intake of water or foods/beverages that did not contain energy were not considered ingestive events. IF was defined as the number of ingestive events in a 24-h period and PS was defined as the energy content of an ingestive event. For this review, the comparison group was set as the group with the lowest IF or PS so that it would be possible to compare the effect of higher versus lower IF and larger versus smaller PS on energy intake and/or body weight. Trials were excluded if they were not primary research (e.g. reviews of literature); were not RCTs; did not report or could not provide body weight change values or values for energy intake upon initiated correspondence with study authors. Interventions that included a cointervention independent of manipulation of IF or PS were included in this review if there was an adequate control group including the cointervention alone. Crossover design trials were included if there was a washout period between treatments and treatment order was randomized. There was no limit restriction on publication date.

The hypothesis centered on how independent changes in IF and/or PS would affect body weight via voluntary alteration in energy intake in a free-feeding environment. Given this hypothesis, it was necessary to separate trials that allowed for ad libitum energy intake from controlled feeding trials where energy intake was tightly controlled according to the study design. There may be a thermodynamic mechanism by which consumption of a controlled diet consisting of larger portions consumed less frequently may have differential effects on body weight compared with an isoenergetic diet consisting of smaller portions consumed more frequently (8, 9). In such trials both IF and PS are manipulated (referred to in this article as IF/PS studies), when energy intake is fixed, an increase in IF would result in a decrease in PS. It is necessary to investigate trials with fixed or prescribed energy intake to determine the effect of such manipulations. Trials that prescribed a controlled feeding regimen that dictated participants' energy intake were not included in the primary analysis but were evaluated separately for the body weight outcome only.

Search Strategy

The systematic review search strategy was implemented by a health sciences librarian using PubMed, Cochrane Central Register of Controlled Trials, CINAHL, and Web of Science Core Collection databases on 26 September, 2018. The same search was conducted again on 22 April, 2019 and 14 April, 2020 for updates. A list of relevant references expected to be generated in the PubMed search was used to validate the search strategy (3, 4, 10–29). Two-thirds of these references were used to develop the search strategy and the remaining one-third was used to validate the search. Text from the titles and abstracts of citations in the development set was entered into VoyantTools, a text-analysis tool, and a

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Supplemental Tables 1–4 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances/.
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Abbreviations used: GRADE, Grading of Recommendations, Assessment, Development and Evaluations; IF, ingestive frequency; PS, portion size; RCT, randomized controlled trial; WMD, weighted mean difference.

TABLE 1 Population, intervention, comparison, outcome, and setting (PICOS) question

Parameter	Description
Population	Healthy individuals (i.e. no hypertension, diabetes, eating disorder diagnosis, no recent change in medications); with normal, overweight or obesity (18 kg/m^2 < BMI <40 kg/m^2)
	Aged 19–65 y
Intervention	Manipulation of portion size and/or ingestive frequency
Comparison	Smaller portion size or lower ingestive frequency treatment arm
Outcomes	Energy intake
	Body weight
Study design	Randomized controlled trial (RCT), crossover or parallel
	Noncontrolled feeding studies
	≥24 h in duration for energy intake, ≥4 wk for body weight

term-frequency analysis was conducted. Terms present at instances of 20% or higher were considered candidate terms and were used to inform the PubMed search strategy. This search strategy was then validated by testing results from the search against the validation set. Separate searches were developed for Cochrane Central Register of Controlled Trials, CINAHL, and Web of Science Core Collection. Search strings are in **Supplemental Table 1**; the searches yielded 9708 results (duplicates removed), which were screened for inclusion in the meta-analysis.

Article Identification and Data Extraction

A multiple-pass method was used to review the articles identified in the database searches (**Figure 1**). The first pass involved screening titles and abstracts by 2 independent reviewers to exclude clearly irrelevant articles. The reviewers crosschecked their results after each pass and differences were discussed and reconciled via an additional reviewer. If there was insufficient information to categorically exclude an article according to the inclusion criteria, the full text of the article was reviewed in the second pass. For the second pass, 2–3 reviewers independently examined the selected articles and extracted data into a template in Excel. Data relevant for the meta-analyses on PS or IF were extracted from the selected trials. Extracted data were reviewed by ≥1 additional reviewer for completeness and accuracy. If a trial was potentially eligible for the meta-analyses, but relevant data were not reported, the trial's authors were contacted via email to acquire unpublished data to determine the trial's eligibility.

Data Synthesis

Trials including multiple intervention arms were treated as distinct interventions. For trials including multiple intervention arms, the arm with the lowest IF or PS was classified as the comparison group.

The mean energy intake values reported in the identified trials were positively associated with their respective SDs. Linear interpolation was used to estimate the SDs for the trials reporting means with missing SDs that were not provided through correspondence with the authors of the respective articles.

Meta-analysis

Random-effects meta-analyses were conducted with StataSE 17 software (StataCorp LP) using the *metan* function and results are reported as the weighted mean differences (WMDs) and 95% CIs. The variance within each comparison was calculated as the squared SEM of the difference. An unpooled SE for mean difference was calculated for parallel arm and crossover studies, treating crossover design studies as if they were parallel studies. This method of calculating SEM assumes that 2 independent groups were included in a trial and uses a correlation factor of 0 (30). This is a conservative method for calculating SEM for crossover design studies, because it results in CIs that are potentially too wide and the trials are weighted lower (31). Therefore, additional analyses were conducted using correlation factors of 0.50 and 0.99 instead of 0 for crossover studies.

Risk of bias

Risk of bias for each article was assessed using "The Cochrane Collaboration's Risk of Bias Tool" version 5.1. Risk of bias was evaluated independently by 3–4 reviewers; discrepancies between reviewers were discussed and resolved by the reviewers.

Heterogeneity and sensitivity analyses

Heterogeneity was assessed using I^2 statistics and significance was set at $P < 0.05$. Sensitivity analyses were performed by removing each study 1 by 1. In addition, a sensitivity analysis was performed to determine if trials that did not report SD (i.e. studies with imputed SD) values influenced the results.

Subgroup analyses

A priori analyses included a plan to conduct a subgroup analysis by BMI (i.e. individuals with normal weight and individuals with overweight/obesity) and trial duration. However, given that the majority of trials included populations with a range of body weights and the short duration of the majority of the trials identified, subgroup analyses were not performed.

For the meta-analysis on IF and energy intake only, posthoc analyses included conducting a subgroup analysis by number of ingestive events in the intervention arm (i.e. 6 or

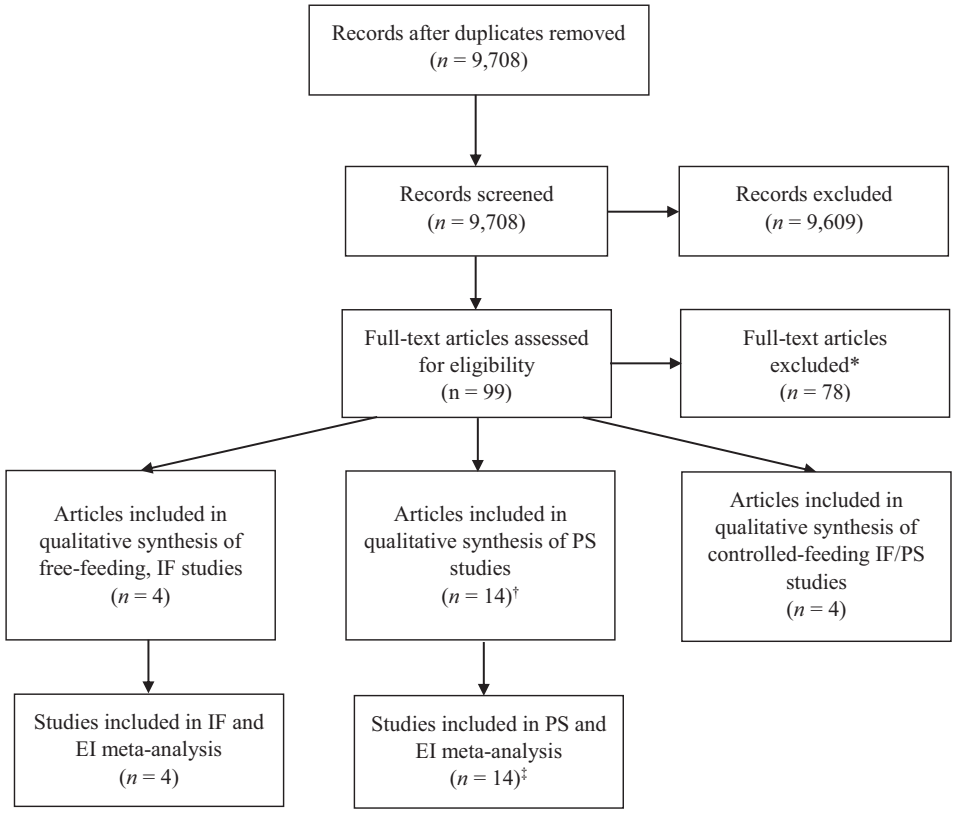

FIGURE 1 Flow diagram of articles included in systematic review. *Exclusion rationale for references included in Supplemental Table 2. †Additional study design information and results for 1 PS and energy intake trial (41) were reported in a publication not identified in the literature search (49); information from this publication was used in this systematic review. ‡Information from 1 trial reported in 2 articles (41, 49); 2 trials reported in 1 article (37). EI, energy intake; IF, ingestive frequency; PS, portion size.

9 events/d compared with 3 events/d) in order to determine a dose-response relation.

Quality of evidence evaluation

The GRADE (Grading of Recommendations, Assessment, Development and Evaluations) Framework was used to evaluate the quality of evidence as high, moderate, low, or very low certainty that the true effect is the effect estimated in the meta-analysis (7). The GRADE rating is based on risk of bias, consistency, directness, publication bias, magnitude of effects, dose response, and opposing plausible residual bias and confounding. The GRADE Framework was designed to evaluate the strength of evidence from randomized, double-blind, placebo-controlled trials, and does not account for the complexity of environmental and behavior exposures of the dietary studies (32). Therefore, the GRADE Framework was slightly modified to not downgrade for the lack of blinding of study participants. This modification was made because it was not always possible to blind participants to PS and IF modifications. In many of the interventions, the visual cue of PS and the temporal cue of IF may contribute to the potential mechanism by which PS and IF influence energy intake and thus should not be blinded. A GRADE rating, evaluated by 2 reviewers, was assigned to each of the intervention types (PS, IF, PS/IF) and outcomes (energy intake, body weight) evaluated in this systematic review.

Results

A total of 9708 articles (duplicates removed) were identified in the literature search. The flow diagram of articles reviewed in the systematic review is summarized in Figure 1. In the first pass, 9609 articles were excluded based on titles and abstracts; 99 articles were retrieved for full-text review in the second pass. A total of 78 articles were excluded in the second pass; rationale for exclusion of each article rejected during the second pass is provided in **Supplemental Table 2**.

Four trials that investigated the effect of IF on free-feeding energy intake were identified (16, 33–35); 14 trials in 13 publications that investigated the effect of PS on free-feeding energy intake were identified (36–48) (**Table 2**). Additional study design information and results for 1 PS and energy intake trial (41) were reported in a publication not identified in the literature search (49); information from this publication was used in this systematic review. Among the trials that investigated the effect of PS or IF on energy intake, 1 trial investigated the effect of IF on body weight (35) and 1 trial investigated the effect of PS on body weight (38) in free-feeding interventions that were ≥4 wk in duration

TABLE 2 Summary of studies examining ingestive frequency (IF) or portion size (PS) and energy intake ≥24 h in duration[1]

Study type	Reference	Study design	Study population	Duration (days)	n[2]	Intervention	Intervention description	Daily energy intake results, kcal (SD)[3]
IF	Farshchi, 2004 (33)	Crossover	F, mean age = 23.7 (7.4) y, NW (BMI between 18 and 24 kg/m^2)	2 (nonconsecutive days)	9	Control	3 ingestive events per day, "irregular" schedule of eating patterns[4]	1759 (136)
						Treatment 1	6 ingestive events per day, "regular" schedule of eating patterns[4]	1902 (189)
						Treatment 2	6 ingestive events per day, "irregular" schedule of eating patterns[4]	1945 (177)
						Treatment 3	9 ingestive events per day, "irregular" schedule of eating patterns[4]	2344 (184)
IF	Farshchi, 2005 (34)	Crossover	F, mean age = 39.9 (5.7) y, OB (BMI between 30 and 40 kg/m^2)	2 (nonconsecutive days)	10	Control	3 ingestive events per day, "irregular" schedule of eating patterns[4]	1857 (134)
						Treatment 1	6 ingestive events per day, "regular" schedule of eating patterns[4]	1907 (117)
						Treatment 2	6 ingestive events per day, "irregular" schedule of eating patterns[4]	2000 (201)
						Treatment 3	9 ingestive events per day, "irregular" schedule of eating patterns[4]	2108 (155)
IF	Johnstone, 2000 (16)	Crossover	M, mean age = 27.3 (6.4) y, NW (BMI between 18 and 24 kg/m^2)	7	8	Control	3 meals with no snacks	3322 (652)[5]
						Treatment 1	3 meals with 3 high-protein snacks (612 kcal total from snacks)	3418 (686)[5]
						Treatment 2	3 meals with 3 high-carbohydrate snacks (624 kcal total from snacks)	3370 (669)[5]
						Treatment 3	3 meals with 3 high-fat snacks (621 kcal total from snacks)	3537 (729)[5]
IF	MacKenzie-Shalders, 2016 (35)	Crossover	M, mean age = 20.1 (1.4) y, BMI not included in inclusion/exclusion criteria	42	24	Control	3 meals per day	3768 (878)
						Treatment	3 meals per day with high-protein beverage (147 kcal) between meals	3773 (785)

(*Continued*)

TABLE 2 (*Continued*)

Study type	Reference	Study design	Study population	Duration (days)	n[2]	Intervention	Intervention description	Daily energy intake results, kcal (SD)[3]
PS	Cheskin, 2008 (36)	Crossover	MF, mean age = 35.5 (NR) y, BMI between 18 and 45 kg/m^2	4	54	Control	Preload meat entrees, 783 kcal	2014 (514)
						Treatment	Preload mushroom entrees, 339 kcal	1640 (476)
PS	De Graaf, 1996—Study 1 (37)	Crossover	MF, mean age = 22 (3) y, NW (BMI <26.0 kg/m^2)	12	48	Control	Standard meal with fat, 1225 kcal, blinded to treatment	F: 2574 (550); M: 3430 (717)
						Treatment	Meal with sucrose polyester fat replacer, 755 kcal, blinded to treatment	F: 2205 (598); M: 2987 (717)
PS	De Graaf, 1996—Study 2 (37)	Crossover	MF, mean age = 22 (3) y, NW (BMI < 26 kg/m^2)	12	47	Control	Standard meal with fat, 1225 kcal, unblinded to fat/fat replacer content	F: 2605 (454); M: 3305 (669)
						Treatment	Meal with sucrose polyester fat replacer, 755 kcal, unblinded to fat/fat replacer content	F: 2215 (550); M: 3058 (693)
PS	French, 2014 (38)	Parallel	MF, mean age = 42.6 (11.2) y, BMI not included in inclusion/exclusion criteria	182[6]	58	Control 1	No lunch provided; instructed to continue their usual lunch patterns	1938 (503)
					57	Control 2	400 kcal lunch	1718 (528)
					59	Treatment 1	800 kcal lunch	1792 (522)
					55	Treatment 2	1600 kcal lunch	1996 (527)
PS	Haynes, 2020 (39)	Crossover	MF, mean age = 31.6 (10.3) y, NW or OW (BMI 22.5–29.8 kg/m^2)	5	30	Control	Normal (i.e. "small-normal") lunch and dinner (543 kcal)	2448 (584)
						Treatment 1	Small (i.e. smaller than normal) lunch and dinner (339 kcal)	2238 (490)
						Treatment 2	Large (i.e. "large-normal") lunch and dinner (747 kcal)	2543 (592)

(*Continued*)

TABLE 2 (*Continued*)

Study type	Reference	Study design	Study population	Duration (days)	n^2	Intervention	Intervention description	Daily energy intake results, kcal (SD)[3]
PS	Hogenkamp, 2012 (49); 2014 (41)	Crossover	MF, mean age = 21 (2.4) y, NW (BMI between 18.0 and 24.0 kg/m^2)	3	27	Treatment 1	Liquid preload, ~99 kcal	1989 (545)[7]
						Treatment 2	Semi-solid preload, ~296 kcal	2133 (563)[7]
						Treatment 3	Liquid preload, ~427 kcal	1985 (431)[7]
						Treatment 4	Semi-solid preload, ~1281 kcal	2827 (436)[7]
PS	Jeffery, 2007 (40)	Crossover	F, mean age = 33 (5.2) y, BMI between 18.5 and 40.0 kg/m^2	20	19	Control	Standard lunch, 750 kcal	1875 (412)[5]
						Treatment	Large lunch, 1500 kcal	2153 (477)[5]
PS	Kelly, 2009 (48)	Crossover	MF, mean age = M: 29.7 (4.6); F: 31.7 (9.5), NW and OW (BMI 18.5–30.0 kg/m^2)	4	43	Control	Standard portions	3119 (702)[5]
						Treatment	Large portions	3531 (798)[5]
PS	Kral, 2004 (42)	Crossover	F, mean age = 23.4 (1 SE) y, NW and OW (BMI 19.0–29.9 kg/m^2)	1	39	Control 1	Preload lunch: 625 kcal, low-energy density (1.25 kcal/g), "sufficient" portion size (500 g)	1671 (302)
						Control 2	Preload lunch: 875 kcal, high-energy density (1.75 kcal/g), "sufficient" portion size (500 g)	1819 (405)
						Treatment 1	Preload lunch: 875 kcal, low-energy density (1.25 kcal/g), moderate portion size (700 g)	1734 (313)
						Treatment 2	Preload lunch: 1125 kcal, low-energy density (1.25 kcal/g), large portion size (900 g)	1763 (320)
						Treatment 3	Preload lunch: 1225 kcal, high-energy density (1.75 kcal/g), moderate portion size (700 g)	1829 (323)
						Treatment 4	Preload lunch: 1575 kcal, high-energy density (1.75 kcal/g), large portion size (900 g)	1947 (351)

(*Continued*)

TABLE 2 (*Continued*)

Study type	Reference	Study design	Study population	Duration (days)	n[2]	Intervention	Intervention description	Daily energy intake results, kcal (SD)[3]
PS	Levitsky, 2011 (43)	Crossover	MF, mean age = 24.8 (8.8) y, BMI not included in inclusion/ exclusion criteria [mean BMI 21.2 (6.2)]	10	17	Control	Ad libitum energy intake	2057 (194)
						Treatment	Low-energy meal replacements, ~200 kcal per meal	1812 (153)
PS	Rolls, 2006a (44)	Crossover	MF, mean age = M: 21.2 (0.5 SE) y, F: 24.4 (1.2 SE) y, NW and OW (BMI 20.0–29.0 kg/m^2)	2	32	Control	Standard ad libitum breakfast, lunch, dinner, and snacks (F: >3000 kcal/d served; M: >3900 kcal/d served)	2582 (667)
						Treatment 1	150% of standard size ad libitum breakfast, lunch, dinner, and snacks (F: >4500 kcal/d served; M: >5850 kcal/d served)	3002 (720)
						Treatment 2	200% of standard size ad libitum breakfast, lunch, dinner, and snacks (F: >6000 kcal/d served; M: >7800 kcal/d served)	3270 (928)
PS	Rolls, 2006b (45)	Crossover	F, mean age = 21.9 (0.7 SE) y, NW – OB (BMI 18.0–40.0 kg/m^2)	2	24	Control 1	Standard energy density (2.11 kcal/g), standard portion size (4304 kcal/d)	2478 (553)[5,8]
						Control 2	Reduced energy density (1.61 kcal/g), standard portion size (3284 kcal/d)	1937 (427)[5,8]
						Treatment 1	Standard energy density (2.11 kcal/g), reduced (75%) portion size (3228 kcal/d)	2225 (494)[5,8]
						Treatment 2	Reduced energy density (1.61 kcal/g), reduced (75%) portion size (2463 kcal/d)	1678 (366)[5,8]

(*Continued*)

TABLE 2 (*Continued*)

Study type	Reference	Study design	Study population	Duration (days)	n^2	Intervention	Intervention description	Daily energy intake results, kcal (SD)[3]
PS	Rolls, 2007 (46)	Crossover	MF, mean age = F: 25.8 (2.7 SE) y, M: 24.7 (1.0 SE), NW and OW (BMI 18.0–30.0 kg/m^2)	11	23	Control	Standard ad libitum breakfast, lunch, dinner, and snacks (F: ~2600 kcal/d; M: ~3300 kcal/d)	2556 (594)
						Treatment	150% of standard size ad libitum breakfast, lunch, dinner, and snacks (F: ~3900 kcal/d; M: ~4950 kcal/d)	2979 (638)
PS	Stroebele, 2009 (47)	Crossover	MF, mean age = 37.3 (12) y, NW – OB (BMI 23.0–40.0 kg/m^2)	7	59	Control treatment	Ad libitum standard size snack packs (187.0–368.5 g/pack)	~2615 (585) kcal/week from snack pack[5,9]
							Ad libitum 100 kcal snack packs (19.2–26.0 g/pack)	~1774 (389) kcal/week from snack pack[5,9]

[1] Means are shown as appropriate with ± SD unless otherwise indicated. F, females; IF, ingestive frequency; M, males; *n*, sample size; NW, normal weight; PS, portion size; OB, obese; OW, overweight.
[2] Sample size included in final analysis.
[3] Values reported as daily energy intake unless otherwise stated.
[4] Farshchi, 2004 (33) and 2005 (34): "subjects were asked to eat and drink similar things to their normal diet, but to either consume them on 6 occasions per day (regular meal pattern) with regular intervals between meals or follow a chaotic eating plan (i.e. irregular meal pattern). To achieve the irregular meal pattern, subjects were asked to have their usual foods and drinks but follow a predetermined meal frequency with between 3 and 9 meals/d for 14 d. Each number of meals per day was repeated twice (i.e. 7, 4, 9, 3, 5, 8, 6, 5, 9, 8, 3, 4, 7, and 6 occasions/d, respectively) with an average of 6 meals/d. The number of meals on the last 2 d of the regular and irregular meal patterns were similar (i.e. 6 and 6 compared with 7 and 6)." Note that "meal" was defined as "any food or snack (solid or liquid) containing energy, with an interval between 2 eating occasions of >1 h."
[5] Jeffery, 2007 (40); Johnstone, 2000 (16); Kelly, 2009 (48); Rolls, 2006b (45); Stroebele et al., 2009 (47): SD estimated using a SDcorr method of imputation.
[6] Five days a week (weekdays) for 6 mo.
[7] Mean energy intake calculated from the mean ad libitum energy buffet from days 1, 2, and 3 plus the energy provided from the test foods reported in Hogenkamp, 2012 (49); SD calculated based on the SD from days 1, 2, and 3.
[8] Rolls, 2006b (45): energy intake data reported as kcal per 2 d. Values divided by 2 to obtain energy intake per day. SD estimated using a SDcorr method of imputation.
[9] Stroebele, 2009 (47): mean calculated based on mean gram intake per treatment group from week 1 and week 2 and kcal/g conversion factors used in the discussion section of publications (840.7 kcal/186.9 g = 4.5 kcal/g). A treatment order effect was reported; "participants receiving standard size packages of snacks during week 2 (who had previously consumed 100 kcal snack packs) consumed an average of only 486.7 g of snacks from the standard size packages, compared with the 675.7 g of snacks consumed by the other randomization group when they received the standard size packages in week 1."

(**Table 3**). Four trials investigated the effect of both IF and PS on body weight among the population of interest for ≥4 wk in controlled feeding trials (i.e. energy intake was fixed between treatments) (25, 50–52) (**Table 4**). Given energy intake was fixed for these 4 trials, differences in energy intake would be attributable to deviations from the trial protocol and thus were considered separately from free-feeding trials in the current review.

RCT characteristics

IF, free-feeding trials.

A summary of the 4 trials investigating the effect of IF on energy intake is provided in Table 2. The trials that manipulated IF ranged from 2 to 42 d in duration and were all crossover designs. Besides the crossover design, these studies varied in other dimensions. One trial randomized normal weight males to consume the following for 7 d in random order: *1*) 3 meals/d, *2*) 3 meals/d with high-protein snacks, *3*) 3 meals/d with high-carbohydrate snacks, and *4*) 3 meals/d with high-fat snacks (16). No significant differences in total daily energy intake over a 7-d timeframe were observed with intake of 3 meals/d with or without high-protein, high-carbohydrate, or high-fat snacks (16). Another trial randomized male rugby players to consume 3 meals/d with and without a high-protein beverage for 42 d (35). No significant differences in total daily energy intake over a 7-d timeframe were observed with intake of 3 meals/d with and without a high-protein beverage between meals for 42 d. This was the only trial that investigated the effect of IF on body weight; body weight was not significantly affected by IF in this invention (35). Two trials employed the same study design among females with normal weight (33) and with obesity (34). In these trials, participants consumed either a "regular" (6 meals/d for 14 d) or "irregular" (3, 6, or 9 meals/d in which the number of meals varied from day to day for 14 d) eating pattern. Energy intake was significantly higher with 9 ingestive events/d during an "irregular" eating pattern (i.e. assigned to consume 3–9 meals/d over the course of 14 d) compared with the consumption of either 3 or 6 meals/d among normal weight females (33). Among females with obesity, consuming 9 meals/d led to higher energy intakes compared with consuming 3 meals, but the difference in energy intake was not significantly different with intake of 3 compared with 6 or 6 compared with 9 meals/d (34).

The effect of high versus low IF on energy intake is displayed in **Table 5**. A random-effects analysis of comparisons between lower versus higher IF revealed a positive association between IF and total daily energy intake. More ingestive events (i.e. 4–9 events compared with 3 events) was associated with intake of an additional 203 kcal/d (95% CI: 76, 330 kcal; $P = 0.002$, $n = 10$). However, the heterogeneity of effects was high ($I^2 = 74.5\%$, $P < 0.001$). Similar WMDs were also observed when a correlation factor of 0.50 (WMD: 194 kcal; 95% CI: 69, 319 kcal; $P = 0.002$; $I^2 = 86.8\%$) or 0.99 (WMD: 173 kcal; 95% CI: 69, 277 kcal; $P = 0.001$; $I^2 = 99.0\%$) were used to calculate SEM for studies with a crossover design. The association remained statistically significant ($P \leq 0.025$) with removal of each individual trial in the sensitivity analysis, but was no longer significant (WMD: 73 kcal; 95% CI: −224, 369; $P = 0.630$, $n = 4$) with the removal of the trials altering IF with "regular" and "irregular" meal patterns (33, 34).

To determine the dose-response relation between ingestive events and energy intake, trials comparing a specific number of ingestive events were analyzed separately. There was only 1 trial that compared 3 versus 4 events/d (35), observing no difference in energy intake. The association between IF and energy intake was statistically significant in the comparison between 3 versus 6 events [117 (50, 184); $P = 0.001$, $n = 7$] and 3 versus 9 events/d [416 (88, 743); $P = 0.013$, $n = 2$]. No trial included treatments with fewer than 3 events/d.

The association between IF and energy intake should be interpreted with caution, given the limited number of trials, the variability of study design in trials that investigated the effect of IF on energy intake, and the high heterogeneity of effects.

Only 1 trial investigated the effect of IF on body weight (Table 3); therefore, a meta-analysis could not be conducted.

PS, free-feeding studies.

The single trial that investigated the effect of PS on both body weight and energy intake was a parallel arm trial among males and females (38). In this trial, PS was manipulated by varying the energy content of the lunch meal 5 d a week for 6 mo (38). The remaining trials investigating the effect of PS on energy intake were crossover design trials and ranged from 1 to 20 d in duration. Some trials altered the PS of ingestive event(s) by: manipulating the macronutrient composition while holding volume constant (i.e. increased/decreased energy density) (37, 42, 44–46), manipulating the amount of food consumed without changing the composition (38–41, 48), restricting energy intake compared with ad libitum intake (43), or manipulating the amount of each food product unit (i.e. increased/decreased amount per package/served) (47). In the trial manipulating unit size (47), only energy intake from snack intake (not total daily energy intake) was reported; thus, undocumented compensatory responses to other sources of energy intake could have occurred. Although some trials were conducted among populations with normal weight (37, 41), the majority of trials investigating the effects of PS were conducted among individuals with normal weight and overweight, individuals with overweight and obesity, or BMI was not specified in the inclusion criteria.

A meta-analysis on PS and energy intake was conducted for all trials identified. However, a meta-analysis on the 1 trial investigating the effect of PS on body weight could not be performed. In the trial investing the effect of PS on body weight, prescribing a 1600 kcal lunch on weekdays for 6 mo resulted in weight gain, but the change in body weight was not significantly different from participants consuming 400 or 800 kcal lunches (38, 41).

TABLE 3 Summary of studies examining ingestive frequency or portion size and body weight ≥4 wk in duration—free feeding[1]

Study type	Reference	Study design	Study population	Duration (days)	Total sample size[2]	Intervention	Intervention description	Baseline BW (kg) or BMI (kg/m^2)[3]	End of intervention BW (kg) or BMI (kg/m^2)[3]
IF	MacKenzie-Shalders, 2016 (35)	Crossover	M, mean age = 20.1 (1.4) y, BMI not included in inclusion/exclusion criteria	42	24	Control	3 meals per day[4]	BW: 102.5 (11.5)	ΔBW: 0.1 (2.4) BW: 102.6 (11.3)
						Treatment	3 meals per day with high-protein beverage (147 kcal) between meals[4]	BW: 102.0 (11.6)	ΔBW: 0.9 (2.5) BW: 102.9 (10.9)
PS	French, 2014 (38)	Parallel	MF, mean age = 42.6 (11.2) y, BMI not included in inclusion/exclusion criteria	182[5]	58	Control	No lunch provided; instructed to continue their usual lunch patterns[4]	BMI: 29.3 (6.4) BW: 84.6 (20.3)	ΔBW: 1.1 (0.42 SE) BW: 86.6 (20.6)
					57	Treatment 1	400 kcal lunch	BMI: 30.9 (6.9) BW: 87.5 (20.5)	ΔBW: −0.1 (0.43 SE) BW: 87.4 (20.4)
					59	Treatment 2	800 kcal lunch	BMI: 30.5 (6.7) BW: 86.6 (20.5)	ΔBW: −0.1 (0.42 SE) BW: 86.6 (20.5)
					55	Treatment 3	1600 kcal lunch	BMI: 28.7 (5.6) BW: 82.9 (17.3)	ΔBW: 1.1 (0.44 SE) BW: 84.4 (17.0)

[1] Means are shown as appropriate with ± SD unless otherwise indicated. BW, body weight, ΔBW, change in body weight from baseline; F, females; IF, ingestive frequency; M, males; PS, portion size.
[2] Sample size included in final analysis.
[3] BW, ΔBW, and/or BMI as provided in the manuscript or from study authors.
[4] Energy content of intervention treatments not reported.
[5] Five days a week (weekdays) for 6 mo.

TABLE 4 Summary of studies examining ingestive frequency and portion size and body weight ≥4 wk in duration—controlled feeding[1]

Study type	Reference	Study design	Study population	Duration (days)	Total sample size[2]	Treatment arm	Intervention description	Baseline BW (kg) or BMI (kg/m^2)[3]	End of intervention BW (kg) or BMI (kg/m^2)[3]
IF/PS	Bachman, 2012 (50)	Parallel, weight loss intervention	MF, mean age = 51.0 (9.9) y, OW and OB (BMI 27.0–45.0 kg/m^2)	180	23	Control	3 meals/d, energy restriction	BMI: 35.7 (4.9)	BMI: 29.8 (4.4)
					22	Treatment	≥100 kcals every 2–3 h, ∼4–6 events/d; energy restriction	BMI: 36.3 (5.4)	BMI: 31.3 (5.3)
IF/PS	Stote, 2007 (25)	Crossover	MF, mean age = 45.0 (0.7) y, NW (BMI 18.0–25.0 kg/m^2)	56	15	Control	3 meals/d, energy intake calculated for weight maintenance	BW: 66.5 (3.1 SE)[4]	BW: 67.3 (3.2 SE)
						Treatment	1 meal/d, energy intake calculated for weight maintenance		BW: 65.9 (3.2 SE)
IF/PS	Verboeket-van de Veene, 1993 (51)	Parallel, weight loss intervention	F, mean age = 46.1 (3.3 SE) y, OW and OB (BMI 25.0–35.0 kg/m^2)	28	7	Control	2 meals/d, energy intake restricted to 1000 kcal/d	BW: 82.2 (4.6 SE)	BW: 78.1 (4.3 SE)
					7	Treatment	3–5 meals/d, energy intake restricted to 1000 kcal/d	BW: 79.0 (2.6 SE)	BW: 74.3 (2.6 SE)
IF/PS	Koopman, 2014 (52)	Parallel	M, mean age 22 (range 19–27) y, NW (mean BMI 22.5, range 19.5–24.5 kg/m^2)	42	8	Control 1	3 meals/d, high-fat/high-sugar beverage consumed with each meal, energy intake calculated for 40% energy surplus	BMI: 22.2 (1.0 SE)	BMI: 22.8 (1.1 SE)
					7	Control 2	3 meals/d, sucrose-sweetened beverage consumed with each meal, energy intake calculated for 40% energy surplus	BMI: 21.9 (1.1 SE)	BMI: 22.7 (1.1 SE)
					8	Treatment 1	6 meals/d, high-fat/high-sugar beverage consumed 2–3 h after meals, energy intake calculated for 40% energy surplus	BMI: 22.5 (1.5 SE)	BMI: 23.4 (1.3 SE)
					8	Treatment 2	6 meals/d, sucrose-sweetened beverage 2–3 h after meals, energy intake calculated for 40% energy surplus	BMI: 22.6 (1.8 SE)	BMI: 23.1 (2.2 SE)

[1] Means are shown as appropriate with ± SD unless otherwise indicated. BW, body weight; F, females; IF, ingestive frequency; M, males; NW, normal weight; OW, overweight; OB, obese; PS, portion size.
[2] Sample size included in final analysis.
[3] BW or BMI as provided in the manuscript.
[4] BW of total study population; baseline BW of treatment and control not reported.

TABLE 5 Meta-analysis of the effect of ingestive frequency on energy intake

Reference	ES (95% CI)	% Weight
Farshchi, 2004—3 irregular vs. 6 irregular (33)	186.0 (40.2, 331.8)	14.05
Farshchi, 2004—3 irregular vs. 6 regular (33)	143.0 (−9.1, 295.1)	13.83
Farshchi, 2004—3 irregular vs. 9 irregular (33)	585.0 (435.5, 734.5)	13.92
Farshchi, 2005—3 irregular vs. 6 irregular (34)	143.0 (−6.7, 292.7)	13.91
Farshchi, 2005—3 irregular vs. 6 regular (34)	50.0 (−60.3, 160.3)	15.26
Farshchi, 2005—3 irregular vs. 9 irregular (34)	251.0 (124.0, 378.0)	14.71
Johnstone, 2000—no snack vs. high-carbohydrate snack (16)	48.0 (−599.2, 695.2)	3.16
Johnstone, 2000—no snack vs. high-fat snack (16)	215.0 (−462.7, 892.7)	2.93
Johnstone, 2000—no snack vs. high-protein snack (16)	96.0 (−559.8, 751.8)	3.09
MacKenzie-Shalders, 2016 (35)	5.0 (−466.2, 476.2)	5.13
Overall ($I^2 = 74.5\%$, $P < 0.001$)	202.9 (75.5, 330.2)	100

ES, effect size.

The forest plot for the effect of lower versus higher PS on energy intake is presented in **Figure 2**. A random-effects analysis of comparisons between lower and higher PS suggested that consumption of larger PSs leads to an increase in total daily energy intake (WMD: 295 kcal; 95% CI: 202, 388 kcal; $P < 0.001$, $n = 24$). However, the heterogeneity of effects was high ($I^2 = 75.4\%$). Similar WMDs were observed and the association remained statistically significant in the

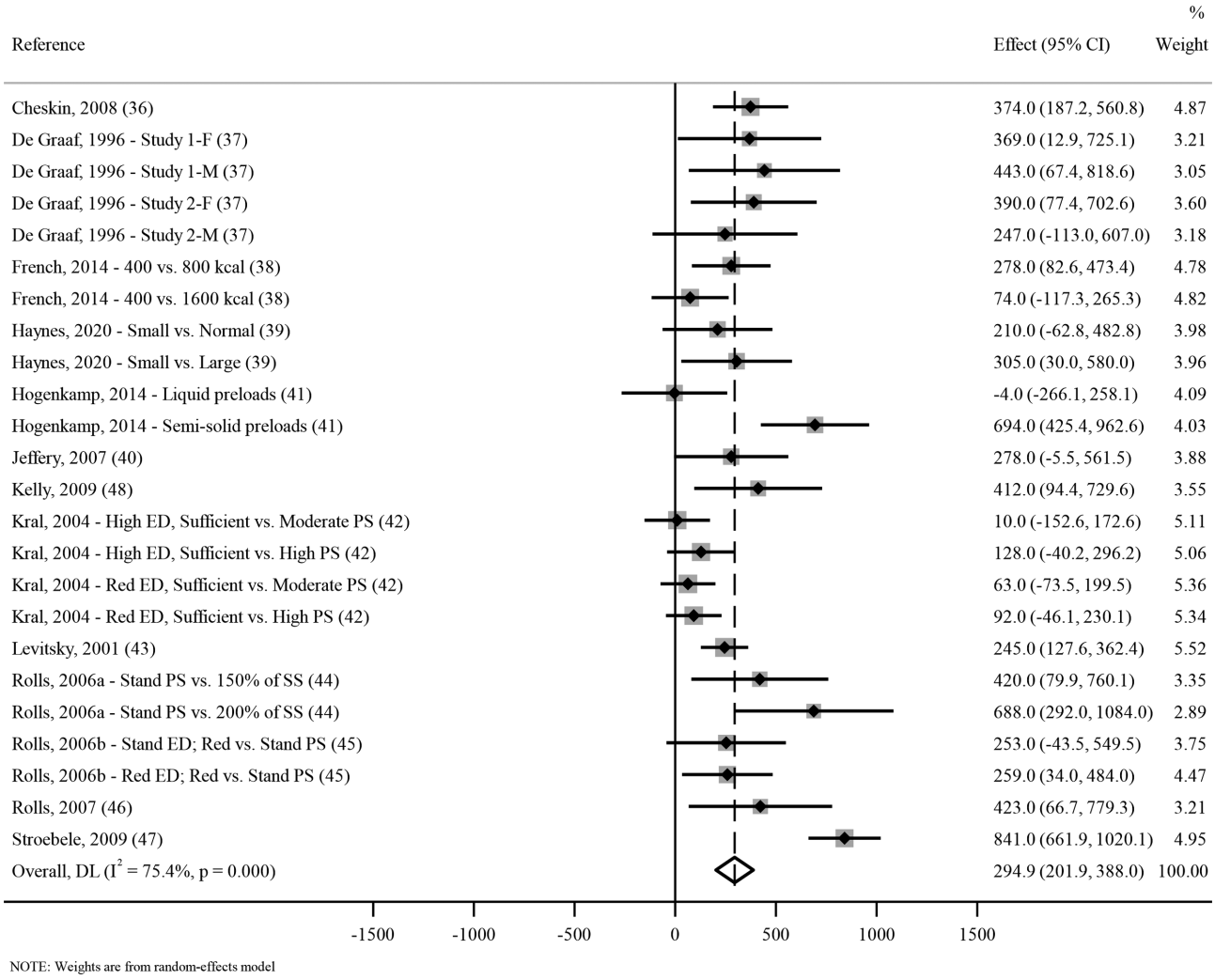

FIGURE 2 Forest plot of the effect of portion size on energy intake. ED, energy density; ES, effect size; F, female; M, male; PS, portion size; Red, reduced; SS, standard size; Stand, standard.

sensitivity analysis with removal of each trial (WMD between 252 and 353 kcal) and removal of all trials with estimated SD when SD or SEM were not reported in the publication (WMD: 248 kcal) (**Supplemental Table 3**). Similar WMDs were also observed when a correlation factor of 0.50 (WMD: 304 kcal; 95% CI: 212, 395 kcal; $P < 0.001$; $I^2 = 86.9\%$) or 0.99 (WMD: 313 kcal; 95% CI: 241, 385 kcal; $P < 0.001$; $I^2 = 99.2\%$) were used to calculate SEM for studies with a crossover design. The difference in PS between the intervention and comparator arm varied widely between trials (an additional 250–1200 kcal/meal or 204–3900 kcal/d), so it was not possible to group trials to determine a dose-response relation or a threshold difference in the energy between treatments associated with significant differences in energy intake.

IF/PS, controlled feeding trials.

The trials that investigated the effect of IF/PS manipulations on body weight in controlled feeding trials prescribed diets with energy intake levels for weight maintenance (25), hypoenergetic diets (50, 51), and hyperenergetic diets (52). Two of the trials were conducted among individuals with normal weight (25, 52) and 2 trials were conducted among populations with overweight/obesity (50, 51). The duration of these trials ranged from 28 to 180 d. The frequency of ingestive events varied across trials and included comparison of body weight in response to 1 versus 3 ingestive events/d (25), 2 versus 3–5 ingestive events/d (51), 3 ingestive events versus an intake of ≥100 kcal every 2–3 h (50), and 3 ingestive events versus 3 ingestive events with 3 beverages consumed between ingestive events (52). Most of these trials allowed the population to select their own foods to consume, but 1 trial provided specific high-sugar or high-fat/high-sugar beverages to consume between main meals (52); another trial provided all foods consumed by the participants (25).

Given the limited number of trials and differences in study design (i.e. energy intake for weight maintenance, hyperenergentic diet, hypoenergetic diet) and the differences in body weight outcomes reported (BMI or body weight), a meta-analysis was not conducted to determine if manipulating IF/PS on isoenergetic diets affects body weight. Among the 4 trials that were ≥4 wk in duration, intake of 3 ingestive events/d resulted in higher body weight compared with 1 ingestive event/d in normal weight participants prescribed energy intake levels for weight maintenance (25). No effect on body weight was observed with hypo- (50, 51) and hyperenergetic diets (52).

Risk of Bias

The Risk of Bias assessment of all relevant trials identified in this review is included in **Supplemental Table 4**. Given the nature of this research, the majority of the authors could not blind participants to the study intervention and outcome assessment, contributing to both performance and detection biases based on Cochrane's Risk of Bias criteria. However, it is important to note that the visual cue of portion and temporal cue of IF may contribute to the potential mechanism by which PS and IF influence energy intake and thus may not be appropriate criteria to evaluate bias of interventions of ingestive behavior. In addition, insufficient information on randomization and allocation concealment was provided in many of the trials to evaluate the risk of selection bias. Risk of attrition bias was unclear for all of the studies that investigated IF and energy intake due to the lack of reporting of participant flow through the study (16, 33, 34) or a high attrition rate (20%) due to injury (35). Among the trials that investigated the effect of PS on energy intake, attrition bias was either unclear (39, 43) or high (41, 46) for 2 trials each. The attrition rate was high (15–30%) for these 4 trials. Attrition bias was high in 2 trials because the analyzed population was based on compliance (46), energy intake (46), and aversion to test foods (41). One IF/PS trial had high risk of attrition bias due to a high attrition rate (29%), with participants reporting dislike of food ($n = 1$ participant) and unwillingness to consume 1 meal/d ($n = 1$) as reasons for discontinuation of the study (25). A treatment order effect was observed in 1 trial that manipulated PS despite a 1-wk washout period (47), suggesting that participants may habituate to reduced PSs. Therefore, the order of treatments in crossover trials may bias the observed effect of PS on energy intake.

Quality of Evidence

A summary of the findings and GRADE quality of evidence for the effect of PS, IF, and PS/IF on energy intake and body weight are presented in **Table 6**.

The quality of evidence on the association between both IF and energy intake and IF and body weight was low and very low, respectively. Although the magnitude of the association between IF and energy intake was high and did follow a dose-response relation, the evidence was inconsistent and based on different IF manipulations. The association was no longer significant with removal of trials that altered IF with "regular" and "irregular" meal patterns (33, 34). The short duration of the interventions also downgrades the quality of evidence on IF and energy intake. Only 1 trial met the inclusion criteria for IF and body weight. This trial was designed to measure the effect of protein supplementation on lean mass changes among rugby players, which indirectly assessed the association between IF and body weight.

The quality of evidence on the association between PS and energy intake was rated as moderate. This stems from the high heterogeneity observed and inability to determine a dose response. The high heterogeneity was attributed largely to the differences in methods used to manipulate PS and the wide variation in energy between the intervention and comparator arms. Additionally, the majority of the trials were <7 d in duration, and thus may lack external validity. The quality of evidence on the association between PS and body weight was very low because only 1 trial met the inclusion criteria for PS and body weight.

TABLE 6 Summary of findings

Ingestive frequency
Population: healthy individuals with normal, overweight, or obesity
Intervention: higher ingestive frequency, free-feeding
Comparison: lower ingestive frequency, free-feeding
Outcomes:

Total *n* (trials)	Estimated effect[1]	Risk of Bias[2]	Consistency of effect	Directness	Precision	Evidence of publication bias	Other considerations	GRADE quality of evidence
Energy intake								
51(4)	203 kcal (75.5, 330.2)	-Unclear selection, detection, attrition, reporting bias[3]	-High heterogeneity ($I^2 = 74.5\%$) -Sensitivity analyses based on design type indicate varying magnitude of effects	-2 studies designed to measure effect of regular compared with irregular eating pattern on energy intake -1 study designed to measure effect of protein supplementation on lean mass among rugby players	Precise	Limited[4]	-Short duration (i.e. ≤7 days) of majority of trials -Large magnitude of effect -Dose response relation observed	Low ⊕⊕◯◯
Body weight								
24(1)	Not estimated; insufficient # of studies	-Unclear selection, detection, attrition bias	NA	-Designed to measure effect of protein supplementation on lean mass -Study conducted among physically active, preseason rugby players; may not be representative of general population	Imprecise	Limited[5]	-Only 1 study identified	Very Low ⊕◯◯◯

(*Continued*)

TABLE 6 (*Continued*)

Portion size
Population: healthy individuals with normal, overweight, or obesity
Intervention: larger portion size, free-feeding
Comparison: smaller portion size, free-feeding
Outcomes:

Total *n* (trials)	Estimated effect[1]	Risk of Bias[2]	Consistency	Directness	Precision	Evidence of publication bias	Other considerations	GRADE quality of evidence
Energy intake								
691(14)	294 kcal (202,388)	-Detection, attrition bias[6] -Unclear selection bias[6] -Treatment order effect observed in 1 trial	High heterogeneity ($I^2 = 75.4\%$)	Portion size manipulated via: -the macronutrient composition while holding volume constant, -the amount of food consumed without changing the composition, -restricting energy intake compared with ad libitum intake, -the amount of each food product unit	Precise	Limited[7]	-Short duration (i.e. ≤7 d) of majority of trials -Large magnitude of effect -Unable to evaluate dose-response relation	Moderate ⊕⊕⊕◯

(*Continued*)

TABLE 6 (*Continued*)

Portion size/ingestive frequency
Population: healthy individuals with normal, overweight, or obesity
Intervention: more frequent, smaller energy ingestive events; controlled feeding
Comparison: less frequent, higher energy ingestive events; controlled feeding
Outcomes:

Total *n* (trials)	Estimated effect[1]	Risk of Bias[2]	Consistency of effect	Directness	Precision	Evidence of Publication Bias	Other considerations	GRADE Quality of Evidence
Body weight								
229(1)	Not estimated; insufficient # of studies	-Selection bias	NA	Direct	Imprecise	None	-Only 1 study identified	Very Low ⊕◯◯◯
105(4)	Not estimated; insufficient # of studies	-Unclear selection, detection bias[8]	NA	1 study prescribed diets for weight maintenance, 2 studies prescribed hypoenergentic diets, and 1 study prescribed hyperenergetic diet	Imprecise[9]	None	None	Very Low ⊕◯◯◯

EI, energy intake; NA, not applicable; WMD, weighted mean difference.
[1] Expressed as WMD (95% CI).
[2] Risk of performance bias due to lack of blinding of participants was not included in this evaluation (see Methods).
[3] Unclear random sequence generation (selection bias) in 4 of 4 trials; unclear allocation concealment (selection bias) in 4 trials; unclear blinding of outcome assessment (detection bias) in 4 trials; unclear incomplete outcome data (attrition bias) in 4 trials; unclear selective reporting in 1 trial.
[4] Two of 4 trials were sponsored by industry; both trials found no statistically significant differences in EI between the greater and fewer ingestive event arms.
[5] Study was sponsored by industry; found no statistically significant differences in EI between the greater and fewer ingestive events.
[6] Unclear random sequence generation (selection bias) in 8 of 14 trials; unclear allocation concealment (selection bias) in 9 trials and high risk in 2 trials; unclear blinding of outcome assessment (detection bias) in 5 trials and high risk in 2 trials; unclear incomplete outcome data (attrition bias) in 2 trials and high risk in 2 trials.
[7] Two of 14 trials were sponsored by industry; both trials produced statistically significant results that were favorable of the sponsored product [i.e. mushrooms (36), sucrose polyester fat replacer (37)].
[8] Unclear random sequence generation (selection bias) in 1 of 4 trials; unclear allocation concealment (selection bias) in 3 trials and high risk in 1 trial; unclear blinding of outcome assessment (detection bias) in 3 trials and high risk in 1 trial; high risk of incomplete outcome data (attrition bias) in 1 trial trials; unclear selective reporting in 1 trial.
[9] Downgraded due to small number of trials ($n \leq 2$) per design type (i.e. weight maintenance, hypo- or hyperenergetic).

The quality of evidence on the association between IF while holding energy intake fixed (IF/PS) and body weight was also very low. Although the effects observed across studies was precise, the differences in study design (i.e. energy intake for weight maintenance, hyperenergentic diet, hypoenergetic diet) limited the ability to synthesize the findings in a meta-analysis. The very low-quality rating is due to the low number of studies with this design type ($n \leq 2$ studies).

Conclusion

Results from these meta-analyses suggest that consuming additional energy, regardless of whether it is driven by additional ingestive events or larger PSs, contributes to increased total daily energy intake. Evidence from RCTs suggests that 6 or more ingestive events/d is associated with increased total daily energy intake compared with 3 events/d; ~76 to 330 kcal additional kcal/d. However, the quality of evidence is low, and the true effect of IF manipulations on energy intake may be markedly different than the effect observed. This association may be attributable simply to increased IF or to an irregular meal pattern (i.e. variable number of meals from day to day) created by additional ingestive events (33, 34). Based on the moderate quality evidence identified, intake of larger portions (an additional 250–1200 kcal per meal or 204–3900 kcal/d) is associated with a net positive intake of ~202 to 388 additional kcal/d. Thus, based on the current limited evidence base, increased IF and PS both account for an additional, ~200–400 kcal/d. These findings suggest that compensation is not precise if either PS or IF are increased.

Given the short duration (i.e. ≤7d) of the majority of the trials identified that investigated PS and IF, it is still unclear whether these differences in energy intake from increased PS or additional ingestive events translate to either a clinically relevant gain in body weight or increased risk of developing other diseases associated with excess food and beverage intake. Previous findings suggest that intraindividual daily energy intake is quite variable, and corrective responses occur over time with deviations in energy intake (53). Therefore, to more accurately evaluate the effect of PS or IF on energy balance, multiple days of monitoring are necessary. Such long-term trials were not identified in this systematic review of the literature.

The positive association between PS and energy intake observed in this meta-analysis has been observed in other reviews. A systematic review on the relation between PS and food consumption concluded that there was moderate quality evidence that larger PSs are associated with increased food consumption among both children and adults, which would theoretically result in a difference of 144 and 228 kcal/d among children and adults, respectively (54). PS in the previous review (54) was defined by a food product's PS, package size, or tableware size or shape, whereas PS was defined by the energy content of an ingestive event in the current review. Despite the difference in definition, the magnitude of effect was similar to, but slightly lower than, the effect observed in the current meta-analysis on PS and energy intake (295 kcal/d). Although the positive association between PS and energy intake was statistically significant, it is unclear if and what threshold difference in PS is necessary to elicit greater total daily energy intake due to the wide range in PS energy content of the control and treatment.

The effect of IF on body composition has also been the topic of recent systematic reviews. The 2020 Dietary Guidelines Advisory Committee conducted a systematic review to identify studies investigating the effect of eating frequency on body composition and risk of overweight and obesity (55). The committee identified 5 cohort studies and 1 RCT (50); the committee's expert opinion was there was insufficient evidence to determine a relation. A previous meta-analysis analyzed the effect of IF on fat and lean mass changes (56). The main finding was an inverse association between meal frequency and body fat percentage. However, the effect was not robust and was attributed to the effects observed in a single trial. The effect of IF on energy intake was not evaluated in either of these reviews.

Several proposed physiological and environmental factors may explain the associations between PS with energy intake. For trials investigating the effects of PS, it has been proposed that isovolumetric portions with varying energy density can achieve similar sensations of satiation due to gastric distension (57). A study design manipulating energy density to change portion was used by 6 of the trials identified in this review (36, 37, 42, 45, 49), 2 of which were designed to determine the interactive effects of energy density and PS (42, 45). Both of these trials (conducted by the same laboratory) reported additive increases in energy intake with the consumption of meals with increased energy density and increased PS. Another proposed mechanism is that unit size can serve as a visual cue that can drive energy intake, as reported in 2 of the PS trials (43, 47). In both trials, food provided in units resulted in significantly decreased total intake compared with ad libitum intake. However, a significant order effect was observed in 1 of these trials (47). The difference in intake between standard packages and portion-controlled packages was no longer statistically significant when participants were initially exposed to the portion-sized packages (47). Others have proposed that PS is not determined by appetitive sensations, but rather by habit or environmental determinants (58), and that neither increases or decreases in PS would result in energy compensation. This hypothesis was tested with varying PSs in the other trials identified (38–40, 44, 46, 48), 3 of which evaluated the dose-response relation between PS and energy intake. In 1 trial, an additional of 800–1600 kcal (but not 400 kcal) at a lunch meal resulted in significantly higher total daily energy intake (38). In another trial, both 400 and 800 additional kcal served per day resulted in significant increases in total daily energy intake (39). Lastly, increasing PS by 150% (~1500 and 1950 additional kcal/d among females and males, respectively) and 200% (~3000 and 3900 additional kcal/d) resulted in significant increases in ad

libitum daily energy intake (44). Results from these studies suggest that energy density, unit size, and volume of the intervention foods and beverages all play a role in how PS affects energy intake in acute studies.

Manipulations in IF are also hypothesized to alter appetitive sensations and energy intake (59). However, contrary to recommendations to consume small, frequent meals to modulate appetite and energy intake, evidence suggests that IF is poorly correlated with appetite ratings. Trials investigating the effects of IF on appetite have reported no association with appetite rating (24, 60) or increased hunger and/or desire to eat (21) with increased IF. Three of the 4 trials identified in this review on IF measured appetitive sensations (16, 33, 34). Mean daily fullness, but not hunger, ratings were significantly different when participants were provided 3 high-protein snacks, 3 high-carbohydrate snacks, 3 high-fat snacks, or no snacks. Fullness ratings were only lower with the no snack condition compared with the high-protein and high-carbohydrate snack condition (16). Conversely, IF had no effect on satiety, hunger, fullness, or prospective consumption ratings among women with normal weight or obesity (33, 34). In short, there are likely a variety of physiological and environmental factors that contribute to the magnitude or lack of effect of IF manipulations on energy intake (58, 59).

We hypothesized that independent increases in PS or IF could affect body weight by altering energy intake. However, there may be a thermodynamic mechanism where altered IF and PS of isoenergetic diets could lead to differential effects on body weight (8, 9). Such an effect was generally not observed among the controlled feeding trials identified in this systematic review. Only 1 of 4 such trials observed a significant difference in body weight (25).

There were many differences in study design among the identified trials, including the number of ingestive events/d for IF trials, method of PS manipulation and magnitude of difference between portions for PS trials, free or controlled feeding, characteristics of the study population (i.e. weight status of participants, gender), and study duration. The impacts of each of these factors on the primary outcomes are unclear due to the small number of trials identified. This hindered the ability to conduct subgroup analyses. Although it is possible to conduct a meta-analysis on a very limited number of trials, its external validity is uncertain, especially if there are substantive differences in study design. In addition, differences in study design may contribute to high heterogeneity of effects.

The present meta-analyses assessed the independent effects of PS and IF on energy intake. However, another question of key importance for setting clinical guidelines and public health policy is whether compensatory responses to IF and PS differ in magnitude, given there is a reciprocal link between PS and IF. Results from these meta-analyses cannot answer whether PS or IF has a more prominent effect on energy intake or body weight. Such a trial would need to hold PS constant and let participants self-select the number of meals they consume. Conversely, IF would need to be held constant while PS would be free to vary. In addition, monitoring appetitive sensations would provide additional information to explain whether differences in energy intake correspond with changes in appetite, a widely assumed mediator. This type of trial may provide insight into whether either PS or IF is a more potent contributor to excess energy intake. Additional RCTs are necessary to determine the long-term effects of changes in IF or PS on body weight.

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